Application No.: 09/744,622 Docket No.: HO-P01615US1

AMENDMENTS TO THE CLAIMS

1. (currently amended) A method for inducing intracellular hyperthermia in a subject comprising the step of administering an amount of a mitochondrial uncoupling agent sufficient to the subject to induce whole body intracellular hyperthermia in the subject.

2. (original) The method of claim 1, wherein the mitochondrial uncoupling agent is 2,4 dinitrophenol.

3. (original) The method of claim 1, wherein the mitochondrial uncoupling agent is selected from the group consisting of. classic uncouplers, including 2,4 dinitrophenol, clofazimine, albendazole, cambendazole, oxibendazole, triclabendazole (TCZ), 6-chloro-5-[2,3- dichlorophenoxyl]-2- methylthio-benzimidazole and their sulfoxide and sulfone metabolites, thiobendazole, rafoxanide, bithionol, niclosamide, eutypine, various lichen acids (hydroxybenzoic acids) such as (+)usnic acid, vulpinic acid and atranorin, 2', 5-dichloro-3-t-butyl- 4'-nitrosalicylanilide (S- 13), 3, 4', 5-trichlorosalicylanilide (DCQ, platanetin, 2-trifluoromethyl-4, 5, 6, 7- tetrachlorobenzimidazole (TTFB), 1799, AU-14 21, 3,4,5,6,9,10-hexahydro- 14,16-dihydroxy-3- methyl-IH-2-benzoxacyclotetradecin-l,7(8H)-dione (zearalenone), N,NI-bis- (4- trifluoromethylphenyl)-urea, resorcylic acid lactones and their derivatives, 3,5-di-t-butyl- hydroxybenzylidenemalononitrile(SF6847), 2,2,-bis (hexafluoroacetonyl) acetone, triphenyl boron, carbonylcyanide 4-trifluoromethoxyphenylhydrazone (FCCP), tributylamine (TBA), carbonyl cyanide 3-chlorophenylhydrazone (CICCP), 1, 3, 6, 8- tetranitrocarbazole, tetrachlorobenzotriazole, 4-iso-octyl-2,6-dinitrophenol(Octyl-DNP), 4- hydroxy-3,5- diidobenzonitrile, mitoguazone (methylglyoxal bisguanylhydrazone), pentachlorophenol (PCP), 5-chloro-2-mercatobenzothiazole (BZT-SH), tribromoimidazole (TBI), N-(3- trifluoromethylphenyl)-anthranilic acid (Flufenamic acid), 4-nitrophenol, 4, 6-dinitrocresol, 4- isobutyl-2,6-dinitrophenol, 2-azido-4-nitrophenol, 5-nitrobenzotriazole, 5-chloro-4- nitrobenzotriazole, tetrachlorobenzotriazole, methyl-o-phenylhydrazone, N-phenylanthranilic acid, N-(3-nitrophenyl)anthranilic acid, N-(2,3-dimethylphenyl) anthranilic acid, mefenamic acid, diflunisal, flufenamix acid, N-(3-chlorophenyl) anthranilic acid, carbonyl cyanide 4-trifluoromethoxyphenylhydrazone (FCCP), SR-4233 (Tirapazamine), atovaquone, carbonyl cyanide 4-(6'-methyl-2'-benzothiazyl)-phenylhydrazone(BT-CCP), ellipticine, olivacine,

ellipticinium, isoellipticine and related isomers, methyl-O-phenylhydrazonocyanoaceticacid,methyl-O-(3-chlorophenylhydrazono) cyanoacetic acid, 2-(3'- chlorophenylhydrazono)-3-oxobutyronitrile, thiosalicylic acid, 2-(2',4-dinitrophenylhydrazono)- 3-oxo-4,4-demethylvaleronitrile, relanium, melipramine, and other diverse chemical entities including unsaturated fatty acids (up to C14 Optimum), sulflaramid and its metabolite perfluorooctane sulfonamide (DESFA), perfluorooctanoate, clofibrate, Wy- 14, 643, ciprofibrate, and fluoroalcohols; ionophorous antibiotic uncouplers, including gramicidin, nigericin, tyrothricin, tyrocidin, valinomycin, alamethicins, harzianin HA V, saturnisporin SA IV, zervarnicins, magainin, cecropins, melittin, hypelcins, suzukacillins, monensins, trichotoxins, antiamoebins, crystal violet, cyanine dyes, cadmium ion, trichosporin-B and their derivatives; and other heterogeneous coupling compounds, including desaspidin, ionized calcium (Ca++), uncoupling proteins such as UCPI-1, UCP-2, UCP-3, PUMP (Plant Uncoupling Mitochondrial Protein), histones, polylysines, A206668-a protein, and compound K23187.

4. (original) The method of claim 1, wherein the mitochondrial uncoupling agent is a conjugate comprising 2,4 dinitrophenol.

5. (currently amended) The method of claim 1, further wherein the induced intracellular hyperthermia is used in the diagnosis or treatment of infections, infestations, malignancies or ~~other medical conditions~~cancer.

6. (canceled)

7. (original) The method of claim 5, wherein the induced intracellular hyperthermia is used in the diagnosis or treatment of cancer.

8. (original) The method of claim 5, wherein an animal is administered the mitochondrial uncoupling agent and a separate medication is administered, wherein the second medication increases the overall metabolic rate of the animal, the metabolic rate of a specific target tissue in the animal, or an increase in free radical flux.

9. (original) The method of claim 8, wherein the second medication is selected from the group consisting of glucagon, arbutamine, dobutamine, vasopressin, glutamine, proline,

octanoate, methylene blue (tetramethylthionine), ubiquinone, menadione, hematoprophyrin, polyunsaturated fatty acids including linoleic (double bonds at carbons 9 and 12), alpha-linolenic (double bonds at carbons 9, 12, and 15), gamma-linolenic (double bonds at carbons 6, 9, and 12), arachidonic (double bonds at carbons 5, 8, 11, and 14), eicosapentaenoic (double bonds at 5, 8, 11, 14, and 17), docosahexenoic (double bonds at carbons 4, 7, 10, 13, 16, and 19), cis-parinaric (double bonds at 9, 11, 13, and 15) and, monounsaturated fatty acids including oleic (double bond at carbon 9), erucic (double bond at carbon 13), phenazine methosulfate, 2,6- dichlorophenolindophenol, coenzyme Q1, CoQ2 and their analogs duroquinone and decylubiquinone.

10. (original) The method of claim 5, wherein the induced intracellular hyperthermia involve the induction of heat shock proteins.

11. (original) The method of claim 5, a second therapeutic agent, or therapy, is administered.

12. (original) The method of claim 11, wherein the second, therapeutic agent or therapy, is selected from the group consisting of- anti-fungal agents, including Amphotericin B, Griseofulvin, Fluconazole (Diflucan), Intraconazole, 5 fluro-cytosine (Flutocytosine, 5-FC), Ketatoconazole and Miconazole; anti-bacterial agents, including beta lactain rings (penicillins), macrocyclic lactone rings (macrolides), polycyclic derivatives of napthacenecarboxamide (tetracyclines), amino sugars in glycosidic linkages (aminoglycosides), peptides (bacitracin, grainicedin, polymixins, etc.), nitrobenzene derivatives of dichloroacedic acid, large ring compounds with conjugated double bond systems (polyenes), various sulfa drugs including those derived from sulfanilamide (sulfonamides, 5-nitro-2-furianyl compounds (nitrofurans), quinolone carboxylic acids (nalidixic acid), fluorinated quinilones (ciprofloxan, enoxacin, ofloxacin, etc.), nitroimidazoles (metroindazole), peptide antibiotics (such as bacitracin, bleomycin, cactinomycin, capreomycin, colistin, dactinomycin, gramacidin A, enduracitin, amphomycin, gramicidin J, mikamycins, polymyxins, stendomycin, actinomycin; aminoglycosides represented by streptomycin, neomycin, paromycin, gentamycin ribostamycin, tobramycin, amikacin; lividomycin beta lactains represented by benzylpenicillin, methicillin, oxacillin, hetacillin, piperacillin, amoxicillin and carbenacillin; lincosaminides represented by

clindamycin, lincomycin, celesticetin, desalicetin; chloramphenicol; macrolides represented by erythromycins, lankamycin, leucomycin, picromycin), nucleosides (such as 5-azacytidine, puromycin, septacidin and amicetin; phenazines represented by myxin, lomofungin, iodin), oligosaccharides (including curamycin and everninomycin; sulfonamides represented by sulfathiazole, sulfadiazine, sulfanilimide, sulfapyrazine) polyenes (including amphotericins, candicidin and nystatin, polyethers tetracyclines (including doxycyclines, minocyclines, methacylcines, chlortetracyclines, oxytetracylcines, demeclocylcines), nitrofurans (including nitrofurazone, furazolidone, nitrofurantoin, furium, nitrovin and nifuroxime), and quinolone carboxylic acids (including nalidixic acid, piromidic acid, pipemidic acid and oxolinic acid); antiviral agents including interferons a, P and 7, amantadine, rimantadine, arildone, ribaviran, acyclovir, abacavir, vidarabine (ARA-A) 9-1,3-dihydroxy-2-propoxy methylguanine (DHPG), ganciclovir, enviroxime, foscarnet, ampligen, podophyllotoxin, 2,3-dideoxytidine (ddQ, iododeoxyuridine (IDU), trifluorothymidine (TIFT), dideoxyMosine (ddi), d4T, 3TC, zidovudine, efavirenz, protease inhibitors such as indinavir, saquinavir, ritonavir, nelfinavir, amprenavir, and specific antiviral antibodies; anti-cancer drugs, including cell cycle-specific agents (including structural analogs or antimetabolites of metholtrexate, mercaptopuorine, fluorouracil, cytarabine, thioguanine, azacitidine), bleomycin peptide antibiotics, such as podophyllin alkaloids including etoposide (VP-16) and teniposide (VM-26), various plant alkaloids such as vincristine, vinblastine, and paclitaxel, anti-neoplastic cell cycle-nonspecific agents such as various alkylating compounds such as busulfan, cyclophosphamide, mechlorethamine, melphalan, altaretarnine, ifosfamide, cisplatin, dacarbazine, procarbazine, lomustine, carmustine, lomustine, semustine, chlorambucil, thiotepa and carboplatin; various hormones, hormone agonists and biologic response modifying agents, including flutamide, prednisone, ethinyl estradiol, diethylstilbestrol, hydroxyprogesterone caproate, medroxyprogesterone, megestrolacetate, testosterone, fluoxymesterone and thyroid hormones such as di-,tri- and tetraiodothyroidine, the aromatase inhibitor, amino glutethimide, the peptide hormone inhibitor octreotide and gonadotropin-releasing hon-none agonists such as goserilin acetate and leuprolide, biologic response modifiers such as various cytokines, interferon alpha-2a, interferon alpha-2b, interferon-gamma, interferon-beta, interleukin-1, interleukin-2, interleukin-4, interleukin-10, monoclonal antibodies (anti-HER-2/neu humanized antibody), tumor necrosis factor, granulocyte-macrophage colony-stimulating factor, macrophage-colony- stimulating factor, various prostaglandins, phenylacetates,

retinoic acids, leukotrines, thromboxanes and other fatty acid derivatives; and radiation therapy.

13. (original) The method of claim 1, wherein the mitochondrial uncoupling agent is an analog of 2,4 dinitrophenol.

14. (original) The method of claim 1, wherein the mitochondrial uncoupling agent is a derivative of 2,4 dinitrophenol.

Claims 15-54 (Canceled)

55. (new) The method of claim 1, wherein the induced intracellular hyperthermia is used to diagnosis or treat atherosclerotic plaques.

56. (new) The method of claim 1, wherein the induced intracellular hyperthermia is used to treat a subject at risk for ischemia and cellular trauma.

57. (new) The method of claim 1, wherein the induced intracellular hyperthermia enhances the immune system of the subject.

58. (new) The method of claim 1, wherein the induced intracellular hyperthermia is used to treat or diagnosis cancer selected from the group consisting of Non-Hodgkin's lymphoma, prostate carcinoma, breast carcinoma, glioblastoma multiforme and Kaposi's sarcoma.

59. (new) The method of claim 1, wherein the induced intracellular hyperthermia is used to treat or diagnosis a carcinoma.

60. (new) The method of claim 60, wherein the carcinoma is peritoneal carcinomatosis, breast carcinoma, or prostate carcinoma.

61. (new) The method of claim 1, wherein the induced intracellular hyperthermia is used to treat or diagnosis a glioma.

62. (new) The method of claim 1, wherein the induced intracellular hyperthermia is used to treat or diagnosis infections that result from Borrelia burgdorferi, Mycobacterium leprae, Treponema pallidum, HIV, hepatitis C, herpes virus or papillomavirus.

63. (new) The method of claim 1, wherein the induced intracellular hyperthermia is used to treat or diagnosis infestations that result from Candida, Sporothrix schenkii, Histoplasma, paracoccidiodes, Aspergillus, Leishmania, malaria, acanthomoeba or cestodes

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